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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,103	12/10/2001	Anthony Boey	20801-000810	3038

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	09/744,103	BOEY ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 12-27-04 is acknowledged.

Claims included in the prosecution are 1-66.

In view of applicant's convincing arguments the previous rejections are withdrawn.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

2. Claims 1-8, 12-13, 15-17, 21-22, 32-39, 43-45, 49, 55, 57 and 59 are rejected under 35 U.S.C. 102(a) as being anticipated by Lee (5,908,777).

Lee discloses compositions containing condensed nucleic acid preparations encapsulated within the liposomes for transfection. The liposomes contain DOPE/PS and PEG-PE. The condensing agent is polylysine, protamine or spermine or spermidine. (abstract, col. 5, line 23 through col. 7, line 64 and examples, Example 1 in particular). The sizes of the liposomes as observed in Fig.3 ranges from 100-200 nm. Although Lee does not specifically state the molecular weight of PEG, PEG-lipid complex in Lee is prepared according to the method of by Lee's previous work wherein PEG 2000 was used.

Lee BBA, 1995 is cited of interest (note materials section).

3. Claims 1-6, 8,12-13, 15-17, 21-22, 28, 32-37, 39, 43-45,49, 55, 57 and 59 are rejected under 35 U.S.C. 102(a) as being anticipated by Martin (5,891,468).

Martin discloses compositions containing condensed nucleic acid preparations encapsulated within the liposomes for transfection. The liposomes contain PE, lipid derivatized with PEG (1-20 mole percent). The sizes of the liposomes range from 100-150 nm (col. 7, lines 14-27, col. 8, lines 18-37, col. 16, line 14 through 65, col. 21, lines 4-21, Examples 9 and 11).

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-8, 12-13, 15-17, 21-22, 32-39, 43-45, 49, 55, 57 and 59 are rejected under 35 U.S.C. 102(a) as being anticipated by Lee (J. Boil. Chem., 1996).

Lee discloses compositions containing condensed nucleic acid preparations encapsulated within the liposomes for transfection. The liposomes contain DOPE/PS and PEG-PE. The condensing agent is polylysine, (abstract and the whole publication). As stated above, although Lee does not specifically state the molecular weight of PEG, PEG-lipid complex in Lee is prepared according to the method of by Lee's previous work wherein PEG 2000 was used.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 11-14, 26-28, 30-31, 42, 52-53, 56, 58 and 62-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee (5,908,777) or Lee (J. Biol. Chem) cited above.

The teachings of Lee (777), Lee (JBC) have been discussed above. What are lacking in Lee are the teachings of the diameters of the complex (condensing agent and the nucleic acid). Since this parameter depends upon the amount of the nucleic acid to be encapsulated, in the absence of showing of unexpected results, it is deemed obvious to one of ordinary skill in the art to manipulate the teachings of Lee with the expectation of obtaining the best possible results. Similarly, instant liposome sizes are deemed to be obvious in view of Lee's teachings on col. 8, line 54 et seq., which the size of the DNA containing liposomes depends on the charge between the complex and the anionic liposomes. Lee also lacks the teachings of the claimed lipid: nucleic acid ratios. This parameter once again is deemed to obvious to one of ordinary skill in the art in view of the relationship between the charge of the complex, the sizes of the liposomes and also because of the nature of the transfection to be carried out. Lee does not teach the addition of the condensing agent in stages or the addition of two condensing agents. However, since the purpose of the condensing agent is to condense the nucleic acid molecule and to protect the nucleic acid from degradation, in the absence of showing unexpected results, such a manipulation is deemed to be within the skill of the art.

7. Claims 17-22, 28-29, 45-48, 53-54, 60 and 63-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee 5,908,777 or Lee, J. Bio. Chem., or Martin (5,891,468) cited above, further in view of Holland (5,885,613).

The teachings of Lee, and Martin have been discussed above. What is lacking in these references is the teaching of PEG ceramide as the bilayer-stabilizing component. What are also lacking in these references are the explicit teachings of the molecular weights of PEG and PEG-lipid amounts in molar percentages.

Holland while disclosing liposomal compositions for the delivery of nucleic acids teaches that PEG when attached to phosphatidylethanolamine (PE) or ceramide (C 14-C20 ceramides) stabilizes the bilayer. The Molecular weight range of PEG is 200-10,000 and the amount of the PEG-lipid is in the range of 0.05 to 30 mole percent (abstract, col. 8, line 60 through col. 9, line 57, col. 24, line 4 through col. 25, line 46 and claims).

The use of PEG-ceramide as the PEG lipid instead of PEG-PE would have been obvious to one of ordinary skill in the art since Holland teaches the effectiveness of both PEG-PE and PEG-ceramide in liposome compositions used in the delivery of nucleic acids. Choosing the appropriate amounts of PEG-lipid and PEG with desired molecular weight with a reasonable expectation of success would have been obvious to one of ordinary skill in the art since Holland teaches manipulations with these parameters.

8. Claims 8-10, 23-25, 39-40, 50-51 and 61are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee (5,908,777), or Lee (J. Biol. Chem), or Martin (5,891,468) cited above, further in view of Lisziewicz (6,420,176).

The teachings of Lee or Martin have been discussed above. What are lacking in these references are the teachings of the use of polyethylenimine as the polycation or the condensing agent.

Lisziewicz while disclosing compositions for delivering DNA into cells teaches that the cationic polymer, polyethylenimine (PEI 25 kD) is effective in binding to DNA and makes a complex and this complex can enter into endosomes of the skin's antigen presenting cells, Langerhans cells, via asialoglycoprotein receptor-mediated endocytosis (abstract, col. 10, line 24 et seq., and claims).

The use of PEI as the polycation in the teachings of Lee or Martin with a reasonable expectation of success since Lisziewicz teaches the ability of this polycation to bind to DNA and effectively enter into endosomes of the skin's antigen presenting cells, Langerhans cells, via asialoglycoprotein receptor-mediated endocytosis.

9. Claims 65-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee 5,908,777 or Lee, J. Bio. Chem., or Martin (5,891,468) cited above, in combination with WO 98/20857 of record.

The teachings of Lee 777, JBC and Martin have been discussed above. What is lacking in these references is the method of preparation of liposomes by reverse phase evaporation method (ethanol injection) or using detergent dialysis.

As pointed out in the previous action, WO 98 discloses liposomal formulations containing nucleic acid complexes and a method of transfection. The nucleic acid is reacted with an organic polycation (spermidine, spermine) to produce a condensed nucleic acid. The composition is further stabilized by the addition of a hydrophilic polymer (PEG). The phospholipids taught by WO include phosphatidic acid, phosphatidylcholine. The liposomes are prepared by using the standard methods of liposomes including detergent dialysis and reverse phase evaporation (abstract, pages 3-4, 7-9, 12, 16-17, 22-25, Examples and claims).

The preparation of liposomes of Lee or Martin by reverse phase evaporation and detergent dialysis methods would have been obvious to one of ordinary skill in the art with a reasonable expectation of success, since these are art known methods as taught by WO.

The reference of Allen (6,120,798) is cited of interest.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK